Remarks

The specification has been amended at pages 29 and 30 to denote the inclusion of registered trademarks, in accordance with M.E.P.E., Rev.1, Feb. 2000, § 608.01(v).

Upon entry of the foregoing amendment, claims 1, 5-7, 9, 13, 14, 16, 18, 21, 25-28, 30, 32-42, 44-47, 50-54, 57, 59-60, 63-72 and 75-78 are pending in the application, with claims 1, 41, 63, 75 and 78 being the independent claims. Claims 2-4, 8, 10-12, 15, 17, 19-20, 22-24, 29, 31, 43, 48-49, 55-56, 58, 61-62 and 73-74 have been canceled without prejudice to or disclaimer of the subject matter therein. Claims 1, 5, 6, 9, 18, 21, 26, 41, 42, 46, 47, 54, 57, 63, 65, 75 and 78 have been amended. Claims 1, 5, 6, 9, 18, 21, 26, 41, 42, 46, 47, 54, 57, and 75 have been amended to restrict the claimed subject matter to the elected invention as traversed. Claims 1, 6, 41, 46 and 75 have been amended to clarify that the terms aryl, carbocyclic, heteroaryl, heterocyclic and compound terms thereof (*e.g.*, arylalkyl) are limited in meaning to the groups described in the specification. Support for the amendment to claims 1, 6, 41, 46, and 75 can be found, *inter alia*, at page 33, line 1, through page 34, line 13, of the application as filed. Claims 63 and 78 have been amended to independent form. Claim 65 has been amended to denote the inclusion of registered trademarks. New claims 79-81 have been added. Support for new claims 79-81 can be found, *inter alia*, at page 33, lines 1-13, of the application as filed.

I. Allowability of the Elected Species

Applicants' note with appreciation the Examiner's statement that "[t]he elected species appears to be allowable." (Office Action, page 5, line 19).

II. Electriction/Restriction

The Examiner has required the election/restriction of the claims under 35 U.S.C. § 121, to one of the following two groups of claims:

I. Claims 1-7, 9, 11-14, 16, 18, 21, 23, 25-28, 30, 32-47, 49-51, 53-54, 57-58, 60, 63-72, drawn to the formula I in claim 1 where Y is CN, A is phenyl or carbocyclic aryl, B is indolo, X is O, Z is NR_8R_9, and R_8 and R_9 are hydrogen; and

II. Claims 1-78, drawn to the formula I in claim 1 where the radicals are all moieties not defined in group I, classified in various classes and subclasses.

(*See* Office Action, page 2, lines 8-15).

Applicants elect the invention of group I for prosecution in the present application. This election is made with traverse. Applicants reserve the right to file one or more applications directed to the subject matter of the non-elected claims.

The Examiner has defined group I to be compounds where Z is NR_8R_9 wherein R_8 and R_9 are hydrogen. (Office Action, page 2, lines 11-12). Applicants traverse to the

extent that expansion of the definition of group I to include compounds where Z is NR_8R_9 wherein R_8 and R_9 are *independently H or* C_{1-4}*alkyl* would not alter the classification of the claimed compounds and would not place an undue burden on the Examiner.

The Examiner has defined group I to be compounds where A is "phenyl or carbocyclic aryl." (Office Action, page 2, lines 10-11). Applicants note that the term "aryl" is used in this application in its normal chemical meaning. *See, e.g., Howley's Condensed Chemical Dictionary, Thirteenth Edition,* John Wiley & Sons, Inc., New York, p. 94, a copy of which is submitted herewith in a Supplemental Information Disclosure Statement as Document AT13 (wherein "aryl" is defined as "[a] compound whose molecules have the ring structure characteristic of benzene, napthalene, phenanthrene, anthracene, etc., (i.e., either the 6-carbon rings of benzene or the condensed 6-carbon rings of the other aromatic derivatives"). Thus, the term "phenyl" is a species within the genus of the term "aryl." Additionally, in this application the adjective "carbocyclic" is not attached to the term "aryl." Such an attachment would be redundant and is therefore unnecessary.

Applicants specifically request that the Examiner advise Applicants if she intended any other meaning for the term "phenyl or carbocyclic aryl."

III. Rejections Under § 112, First Paragraph

A. Claims 1-7, 9, 11-14, 16, 18, 21, 23, 25-28, 30, 32-47, 49-51, 53-54, 57-58, 60, 63-72 and 75-78

The Examiner has rejected claims 1-7, 9, 11-14, 16, 18, 21, 23, 25-28, 30, 32-47, 49-51, 53-54, 57-58, 60, 63-72 and 75-78 under 35 U.S.C. § 112, first paragraph. (Office Action, page 3, lines 20-21). Applicants respectfully traverse this rejection.

Specifically, the Examiner is of the opinion that:

> [T]he specification does not reasonably provide enablement for the radicals Rx and Ry of formula I in claim 1 taken together with nitrogen to form all heterocycles, R8 and R9 combined together with the group attached to them to form all heterocycles, A equal to all aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl groups, and B equal to all optionally substituted aromatic rings or all optionally substituted heteroaromatic rings. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement. The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. The applicant is referred to ***In re Wands,*** 858 f.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988) which includes the incorporation of the 8 factors recited in ***Ex parte*** forman 230 USPQ 546 (Bd. Of App. And Inter 1986).

(Office Action, page 3, line 21, through page 4, line 12). Applicants respectfully disagree.

Claims 2-4, 11-12, 23, 43, 49 and 58 have been canceled. Claims 1, 41, 46 and 75 have been amended such that the terms R_x and R_y do not occur. Claims 5-7, 9, 13-14, 16, 18, 21, 25, 30, 32-40, 42, 44-45, 47, 50-51, 53-54, 57, 60, 63-72, and 76-78 do not

contain R_x or R_y. Therefore, none of the rejected claims is indefinite in view of the terms R_x and R_y.

Claims 1, 41 and 75 have been amended such that R_8 and R_9 are independently H or C_{1-4}alkyl. Claim 46 has been amended such that the terms R_8 and R_9 do not occur. The terms R_8 and R_9 do not occur in any of claims 5-7, 9, 13-14, 16, 18, 21, 25, 30, 32-40, 42, 44-45, 47, 50-51, 53-54, 57, 60, 63-72 and 76-78. Therefore, none of the rejected claims is indefinite in view of the terms R_8 and R_9.

Claims 1, 6, 41, 46 and 75 have been amended to clarify that the terms aryl, heteroaryl, carbocyclic, heterocyclic and compound terms thereof (*e.g.*, arylalkyl) are limited in meaning to the groups described in the specification. The terms saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic and partially saturated heterocyclic do not appear in amended claims 1, 6, 41, 46 and 75. Therefore claims 1, 6, 41, 46 and 75 are not indefinite.

Claims 5-7, 9, 13-14, 16, 18, 21, 25, 30 and 32-40 are dependent, directly or indirectly, upon claim 1. Claims 42, 44-45, 47, 50-51, 53-54, 57, 60 and 63-72 are dependent, directly or indirectly, on claim 41. Claims 76-77 are dependent, directly or indirectly, on claim 75. Amended claim 78 is an independent compound claim. Therefore, none of the rejected claims is indefinite in view of the terms aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic and arylalkyl.

In compliance with the restriction requirement (*see* Office Action, page 2, line 8, through page 3, line 5), claims 1, 41 and 75 been amended so that B is an optionally

substituted indolo ring. The term B does not occur in any of claims 5-7, 9, 13-14, 16, 18, 21, 25, 30, 32-40, 42, 44-47, 50-51, 53-54, 57, 60, 63-72 and 76-78. Therefore, none of the rejected claims is indefinite in view of the term B.

Applicants respectfully submit that the rejection of claims 1-7, 9, 11-14, 16, 18, 21, 23, 25-28, 30, 32-47, 49-51, 53-54, 57-58, 60, 63-72 and 75-78 under 35 U.S.C. § 112, first paragraph, has been accommodated and should be withdrawn.

B. Claim 28

The examiner has rejected claim 28 under 35 U.S.C. § 112, first paragraph. (Office Action, page 4, line 13). Applicants respectfully traverse this rejection.

Specifically, the Examiner is of the opinion that:

> [T]he specification, does not reasonably provide enablement for the method of treating all of the various cancers mentioned. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.

(Office Action, page 4, lines 13-18). Applicants respectfully disagree with the Examiner's analysis and conclusions.

The specification provides explicit enablement for the formulation of pharmaceutical preparations (*see, e.g.,* page 45, line 16, through page 47, line 31). The specification further provides explicit enablement for dosages and methods of

administration (*see, e.g.*, page 43, line 23, through page 44, line 24). The specification also describes a method for treating cancer:

> wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, malignant melanoma, choriocarcinoma, mycosis fungoides, head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma.

See, e.g., the paragraph bridging pages 37 and 38 of the application as filed.

The Examiner is of the opinion that "[t]he specification, does not reasonably provide enablement for the method of treating *all* of the various cancers mentioned." (Office Action, page 4, lines 13-15) (emphasis added). The implication is that the Examiner is of the opinion that the specification enables the treatment of some of the cancers listed in claim 28 but not others. However, the Examiner has provided no evidence in support of her opinion. The Examiner's further statements ("The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.") (Office Action, page 4, lines 15-18) merely state the conclusion. These statements do not provide any

evidence as to why one of ordinary skill in the art would be of the opinion that the full scope of claim 28 is not enabled.

"[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). *See also* M.P.E.P., Rev. 1, Feb. 2000, § 2164.04 ("Burden on the Examiner Under the Enablement Requirement"). Applicants respectfully submit that the Examiner has not met the burden of establishing a *prima facie* case for non-enablement of claim 28, under 35 U.S.C. § 112, first paragraph, and the rejection should be withdrawn.

IV. Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 1 under 35 U.S.C. § 112, second paragraph. (*See* Office Action, page 5, lines 3-17). Applicants respectfully traverse this rejection.

A. The First Stated Grounds for Rejecting Claim 1, Under 35 U.S.C. § 112, Second Paragraph

The Examiner is of the opinion that "[i]n claim 1, line 13, the phrase 'Rx and Ry are taken together with the nitrogen to form a heterocycle' is indefinite because it is so broad. All other occurrences of the term 'heterocycle' in claim 1 are also indefinite.

Which heterocycle is the applicant claiming?" (Office Action, page 5, lines 6-9). Applicants respectfully disagree.

Claim 1 has been amended such that the terms R_x, R_y and heterocycle do not occur. Therefore, claim 1 is not indefinite.

B. The Second Stated Grounds for Rejecting Claim 1, Under 35 U.S.C. § 112, Second Paragraph

The Examiner is of the opinion that: "[i]n claim 1, lines 18-20, the phrase 'A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl is indefinite. Terms such as 'heteroaryl' are so broad as to render the claim meaningless. What heteroaryl rings, for example is the applicant claiming?" (Office Action, page 5, lines 10-14). Applicants respectfully disagree.

Claim 1 has been amended to clarify that the term aryl means C_{6-14}aryl. The terms heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic and arylalkyl do not occur in amended claim 1. Therefore, claim 1 is not indefinite in view of the terms aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic and arylalkyl.

C. The Third Stated Grounds for Rejecting Claim 1, Under 35 U.S.C. § 112, Second Paragraph

The Examiner is of the opinion that "[i]n claim 1, lines 21-22, the phrase 'B is an optionally substituted aromatic ring or an optionally substituted heteroaromatic ring' is indefinite. What aromatic ring or heteroaromatic ring is the applicant claiming?" (Office Action, page 5, lines 15-17). Applicants respectfully disagree.

Claim 1 has been amended such that the phrase "B is an optionally substituted aromatic ring or an optionally substituted heteroaromatic ring" does not occur. In compliance with the restriction requirement (*see* Office Action, page 2, line 8, through page 3, line 5), claim 1 has been amended so that B is an optionally substituted indolo ring. Therefore, claim 1 is not indefinite in view of the term B.

D. Conclusion

Applicants respectfully submit that all of the stated grounds for the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, have been accommodated and the rejection should be withdrawn.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

In the specification:

The paragraph bridging pages 38 and 39 has been amended as follows:

Another embodiment of the present invention is directed to a composition effective to inhibit neoplasia comprising a compound, or a pharmaceutically acceptable salt or prodrug of said compound of Formulae I-IV, which functions as a caspase cascade activator and inducer of apoptosis, in combination with at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent. Examples of known anti-cancer agents which can be used for combination therapy include, but are not limited to, alkylating agents such as busulfan, cis-platin, mitomycin C, and carboplatin; antimitotic agents such as colchicine, vinblastine, paclitaxel, and docetaxel; topo I inhibitors such as camptothecin and topotecan; topo II inhibitors such as doxorubicin and etoposide; RNA/DNA antimetabolites such as 5-azacytidine, 5-fluorouracil and methotrexate; DNA antimetabolites such as 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea and thioguanine; antibodies such as [Herceptin] Herceptin® and [Rituxan] Rituxan®. Other known anti-cancer agents which can be used for combination therapy include melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine,

mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen and alanosine.

The paragraph bridging pages 39 and 40 has been amended as follows:

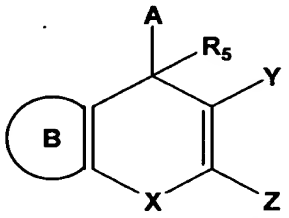
Another embodiment of the present invention is directed to a composition effective to inhibit neoplasia comprising a bioconjugate of said compound of Formulae I-IV, which functions as a caspase cascade activator and inducer of apoptosis, in bioconjugation with at least one known therapeutically useful antibody, such as [Herceptin] Herceptin® or [Rituxan] Rituxan®, growth factors such as DGF, NGF, cytokines such as IL-2, IL-4, or any molecule that binds to the cell surface. The antibodies and other molecules will deliver compound of Formulae I-V to its target and make them effective anticancer agents. The bioconjugates also could enhance the anticancer effect of therapeutically useful antibodies, such as [Herceptin] Herceptin® or [Rituxan] Rituxan®.

In the claims:

Claims 2-4, 8, 10-12, 15, 17, 19-20, 22-24, 29, 31, 43, 48-49, 55-56, 58, 61-62 and 73-74 have been canceled without prejudice or disclaimer.

Claims 1, 5, 6, 9, 18, 21, 26, 41, 42, 46, 47, 54, 57, 63, 65, 75 and 78 have been amended as follows:

1. (once amended) A method of treating a disorder responsive to the induction of apoptosis in an animal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

X is O [or S];

Y is CN[, COR_7, CO_2R_7 or $CONR_xR_y$, wherein R_7, R_x and R_y are independently hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or

R_x and R_y are taken together with the nitrogen to form a heterocycle];

Z is NR_8R_9, [$NHCOR_8$, $N(COR_8)_2$, $N(COR_8)(COR_9)$, $N{=}CHOR_8$ or $N{=}CHR_8$,] wherein R_8 and R_9 are [independently] H[,] or C_{1-4} alkyl [or aryl, or R_8 and R_9 are combined together with the group attached to them to form a heterocycle];

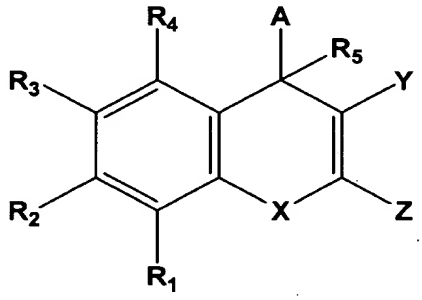
R_5 is hydrogen or C_{1-10} alkyl;

A is optionally substituted [and is] $\underline{C_{6\text{-}14}}$ aryl[, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl]; and

B is an optionally substituted [aromatic ring or an optionally substituted heteroaromatic] indolo ring.

5. (once amended) The method of claim 1, wherein A is optionally substituted [and selected from the group consisting of] phenyl[, napthyl, quinolyl, isoquinolyl, pyridyl, thienyl, furyl, pyrrolyl, 2-phenylethyl and cyclohexyl].

6. (once amended) The method of claim 1, wherein said compound has the Formula II:



(II)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

(a) R_1-R_4 are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, $C_{1\text{-}10}$ alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy,

carbonylamido or alkylthiol; [or] and R_1 and R_2, or R_2 and R_3, or R_3 and R_4, taken together with the atoms to which they are attached form [an aryl, heteroaryl, partially saturated carbocyclic or partially saturated heterocyclic] a pyrrolo group, wherein said group is optionally substituted;

(b) the aryl portion of said arylalkyl, the aryl portion of said arylalkenyl and the aryl portion of said arylalkynyl are each independently C_{6-14} aryl;

(c) said carbocyclic is C_{3-8} cycloalkyl or C_{3-8} cycloalkenyl;

(d) said heteroaryl, the heteroaryl portion of said heteroarylalkyl, the heteroaryl portion of said heteroarylkenyl and the heteroaryl portion of said heteroarylalkynyl are each independently selected from the group consisting of thienyl, benzo[b]thienyl, naphtho[2,3-b]thienyl, thianthrenyl, furyl, pyranyl, isobenzofuranyl, chromenyl, xanthenyl, phenoxanthiinyl, 2*H*-pyrrolyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolizinyl, isoindolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl, 4*H*-quinolizinyl, isoquinolyl, quinolyl, phthalzinyl, naphthyridinyl, quinozalinyl, cinnolinyl, pteridinyl, carbazolyl, β-carbolinyl, phenanthridinyl, acrindinyl, perimidinyl, phenanthrolinyl, phenazinyl, isothiazolyl, phenothiazinyl, isoxazolyl, furazanyl, phenoxazinyl, 1,4-dihydroquinoxaline-2,3-dione, 7-aminoisocoumarin, pyrido[1,2-a]pyrimidin-4-one, 1,2-benzoisoxazol-3-yl, benzimidazolyl, 2-oxindolyl 2-oxobenzimidazolyl and the N-oxides thereof; and

(e) said heterocyclic and the heterocyclic portion of said heterocycloalkyl are each independently selected from the group consisting of tetrahydrofuranyl, pyranyl, piperidinyl, piperazinyl, pyrrolidinyl, imidazolidinyl, imidazolinyl, indolinyl,

isoindolinyl, quinuclidinyl, morpholinyl, isochromanyl, chromanyl, pyrazolidinyl pyrazolinyl, tetronoyl and tetramoyl.

9. (once amended) The method of claim 6, wherein R_1 and R_2, or R_2 and R_3, or R_3 and R_4, are taken together to form a structure selected from the group consisting of [–O–CH_2–O–, –$(CH_2)_3$–, –$(CH_2)_4$–, –O–CH_2CH_2–O–,] –$CH_2N(R)CH_2$–, [–$CH_2CH_2N(R)CH_2$–, –$CH_2N(R)CH_2CH_2$–,] –N(R)–CH=CH–[,] and –CH=CH–N(R)–, [–O–CH=CH–, –CH=CH–O–, –S–CH=CH–, –CH=CH–S– and –N=CH–CH=N–,] wherein R is hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

18. (once amended) The method of claim 16, wherein R_1 and R_2, or R_2 and R_3, or R_3 and R_4, are taken together to form a structure selected from the group consisting of [–OCH_2O–, –$(CH_2)_3$–, –$(CH_2)_4$–, –OCH_2CH_2O–,] –$CH_2N(R)CH_2$–, [–$CH_2CH_2N(R)CH_2$–, –$CH_2N(R)CH_2CH_2$–,] –N(R)–CH=CH–[,] and –CH=CH–N(R)–, [–O–CH=CH–, –CH=CH–O–, –S–CH=CH–, –CH=CH–S– and –N=CH–CH=N–,] wherein R is hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

21. (once amended) The method of claim 16, wherein R_1 and R_2 together form an optionally substituted ring, wherein said ring is [selected from the group consisting of benzo, pyrido, furo, thieno,] pyrrolo[, imidazolo and pyrazo].

26. (once amended) The method of claim 1, wherein said compound is selected from the group consisting of:

[2-Amino-3-cyano-7-dimethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(1-naphthyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-naphthyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4-methoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,6-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4-fluorophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4,5-trimethoxyphenyl)-4*H*-chromene;

2-Acetamido-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4*H*-chromene;

2-Di(ethoxycarbonyl)amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-diethylamino-4-(3-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-methyl-3-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethylphenyl)-4*H*-chromene;

3-Cyano-7-dimethylamino-4-(4,5-methylenedioxyphenyl)-2-propionamido-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-methoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-diethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenyl-4*H*-chromene;

2-Benzylidenamino-3-cyano-7-dimethylamino-4-phenyl-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-cyclohexyl-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-3-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,4,5-trifluorophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3,4-trifluorophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-3-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-ethylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-fluoro-3-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-6,7-methylenedioxy-4-(3-methoxy-4,5-methylenedioxy-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-ethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-4-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoromethylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-furyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-thienyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-6-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-phenoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-phenylethyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3-difluoro-4-trifluoromethylphenyl)-4*H*-chromene;

2,7-Diamino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-(4-methoxyphenoxy)phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dichlorophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-quinolyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-quinolyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenylmethyl-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-carboxaldehydephenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-bromo-3,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-7-acetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

2,7-Diamino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-6,7,8,9,10,11-hexahydro-4*H*-pyrido[3,2,1-ij]quino[5,6-b]pyran;]

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-b]pyran;

[2-Amino-3-cyano-7-ethylamino-6-methyl-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2,7-Diamino-3-cyano-8-methyl-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-7-chloroacetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;]

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

[2-Amino-3-cyano-7-dimethylamino-4-(3-bromophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dibromophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyanophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chlorophenyl)-4*H*-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-naphtho[1,2-b]pyran;]

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4*H*-indolo[4,5-b]pyran;

[2-Amino-3-cyano-7-dimethylamino-4-(3-methoxyphenyl)-4*H*-chromene;]

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4*H*-indolo[4,5-b]pyran;

[2-Amino-3-cyano-7-dimethylamino-4-(3,5-difluorophenyl)-4*H*-chromene;]

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

[2-Amino-3-cyano-7-dimethylamino-4-(3,5-bis(trifluoromethyl)phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-5-methoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-4-(4-bromo-3,5-dimethoxyphenyl)-4*H*-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-methoxy-4,5-methelenedioxyphenyl)-4*H*-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4*H*-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyano-4-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-nitro-4-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylthiophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-difluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-hydroxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylaminophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-dimethylaminophenyl-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-iodo-4,5-dimethoxyphenyl)-4H-naptho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3-indo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-4,5-dimethoxyphenyl)-4H-chromene;

2-Chloroacetamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Acrylamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

3-Cyano-7-dimethylamino-2-succinimido-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

3-Cyano-7-dimethylamino-2-phenylureido-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;] and

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran[;

2-Amino-3-cyano-7-dimethylamino-4-(5-bromo-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-2-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-naphtho[2,1-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-2-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-isoquino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quino[8,7-b]pyran;

2-Amino-3-cyano-7-ethoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8,9,10-tetrahydro-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8-dimethyl-4H-chromene;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl-4H-quino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-6-chloro-3-cyano-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-methoxy-4-(3,4,5-trimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-cyanophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-chlorophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-bromophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methoxy-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methylthio-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-chloro-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-bromo-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methyl-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-chloro-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-bromo-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-bromo-4-(5-methyl-3-pyridyl)-4H-chromene;

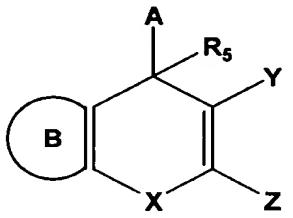
2-Amino-3-cyano-7-chloro-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-ethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-ethylamino-4-(5-methyl-3-pyridyl)-4H-chromene; and

2-Amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene].

41. (once amended) A pharmaceutical composition comprising a pharmaceutically acceptable excipient or carrier and a compound of Formula I:



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

X is O [or S];

Y is CN[, COR_7, CO_2R_7 or $CONR_xR_y$, wherein R_7, R_x and R_y are independently hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R_x and R_y are taken together with the nitrogen to which they are attached to form a heterocycle];

Z is NR_8R_9,[$NHCOR_8$, $N(COR_8)_2$, $N(COR_8)(COR_9)$, $N{=}CHOR_8$ or $N{=}CHR_8$,] wherein R_8 and R_9 are independently H[,] or C_{1-4} alkyl [or aryl, or R_8 and R_9 are combined together with the group attached to them to form a heterocycle];

R_5 is hydrogen or C_{1-10} alkyl;

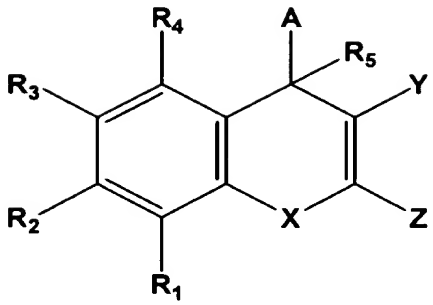
A is optionally substituted [and is] C_{6-14} aryl[, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl]; and

B is an optionally substituted [aromatic ring or an optionally substituted heteroaromatic] indolo ring[;

with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, napthyl, thienyl, pyridyl, benzothienyl, quinolinyl, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen].

42. (once amended) The pharmaceutical composition of claim 41, wherein [B is optionally substituted and selected from the group consisting of benzo, naphtho, indolo, quino and isoquino and] A is optionally substituted [and selected from the group consisting of] phenyl[, naphthyl, pyridyl, quinolyl, isoquinolyl, thienyl, furyl, pyrrolyl, 2-phenylethyl and cyclohexyl].

46. (once amended) The pharmaceutical composition of claim 41, comprising a pharmaceutically acceptable excipient or carrier and a compound of Formula II:



(II)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

(a) R_1-R_4 are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C_{1-10} alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; [or] and

R_1 and R_2, or R_2 and R_3, or R_3 and R_4, taken together with the atoms to which they are attached form [an aryl, heteroaryl, partially saturated carbocyclic or partially saturated heterocyclic] a pyrrolo group, wherein said group is optionally substituted[;

X is O or S;

Y is CN, COR_7, CO_2R_7 or $CONR_xR_y$, wherein R_7, R_x and R_y are independently hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R_x and R_y are taken together with the nitrogen to which they are attached to form a heterocycle;

Z is NR_8R_9, $NHCOR_8$, $N(COR_8)_2$, $N(COR_8)(COR_9)$, $N{=}CHOR_8$ or $N{=}CHR_8$, wherein R_8 and R_9 are independently H, C_{1-4} alkyl or aryl, or R_8 and R_9 are combined together with the group attached to them to form a heterocycle;

R_5 is hydrogen or C_{1-10} alkyl; and

A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl;

with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, napthyl, thienyl, pyridyl, benzothienyl, quinolinyl, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen].

(b) the aryl portion of said arylalkyl, the aryl portion of said arylalkenyl and the aryl portion of said arylalkynyl are each independently C_{6-14} aryl;

(c) said carbocyclic is C_{3-8} cycloalkyl or C_{3-8} cycloalkenyl;

(d) said heteroaryl, the heteroaryl portion of said heteroarylalkyl, the heteroaryl portion of said heteroarylkenyl and the heteroaryl portion of said heteroarylalkynyl are each independently selected from the group consisting of thienyl, benzo[b]thienyl, naphtho[2,3-b]thienyl, thianthrenyl, furyl, pyranyl, isobenzofuranyl, chromenyl, xanthenyl, phenoxanthiinyl, 2*H*-pyrrolyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolizinyl, isoindolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl, 4*H*-quinolizinyl, isoquinolyl, quinolyl, phthalzinyl, naphthyridinyl, quinozalinyl, cinnolinyl, pteridinyl, carbazolyl, β-carbolinyl, phenanthridinyl,

acrindinyl, perimidinyl, phenanthrolinyl, phenazinyl, isothiazolyl, phenothiazinyl, isoxazolyl, furazanyl, phenoxazinyl, 1,4-dihydroquinoxaline-2,3-dione, 7-aminoisocoumarin, pyrido[1,2-a]pyrimidin-4-one, 1,2-benzoisoxazol-3-yl, benzimidazolyl, 2-oxindolyl 2-oxobenzimidazolyl and the N-oxides thereof; and

(e) said heterocyclic and the heterocyclic portion of said heterocycloalkyl are each independently selected from the group consisting of tetrahydrofuranyl, pyranyl, piperidinyl, piperazinyl, pyrrolidinyl, imidazolidinyl, imidazolinyl, indolinyl, isoindolinyl, quinuclidinyl, morpholinyl, isochromanyl, chromanyl, pyrazolidinyl pyrazolinyl, tetronoyl and tetramoyl.

47. (once amended) The pharmaceutical composition of claim 46, wherein R_1 and R_2, or R_2 and R_3, or R_3 and R_4, are taken together to form a structure selected from the group consisting of [$-OCH_2O-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-OCH_2CH_2O-$,] $-CH_2N(R)CH_2-$, [$-CH_2CH_2N(R)CH_2-$, $-CH_2N(R)CH_2CH_2-$,] $-N(R)-CH=CH-$[,] and $-CH=CH-N(R)-$, [$-O-CH=CH-$, $-CH=CH-O-$, $-S-CH=CH-$, $-CH=CH-S-$ and $-N=CH-CH=N-$,] wherein R is hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

54. (once amended) The pharmaceutical composition of claim 53, wherein R_1 and R_2, or R_2 and R_3, or R_3 and R_4, are taken together to form a structure selected from

the group consisting of [$-OCH_2O-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-OCH_2CH_2O-$,] $-CH_2N(R)CH_2-$, [$-CH_2CH_2N(R)CH_2-$, $-CH_2N(R)CH_2CH_2-$,] $-N(R)-CH=CH-$[,] and $-CH=CH-N(R)-$, [$-O-CH=CH-$, $-CH=CH-O-$, $-S-CH=CH-$, $-CH=CH-S-$ and $-N=CH-CH=N-$,] wherein R is hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

57. (once amended) The pharmaceutical composition of claim 53, wherein R_1 and R_2 together form an optionally substituted ring, wherein said ring is [selected from the group consisting of benzo, pyrido, furo, thieno,] pyrrolo[, imidazo and pyrazo].

63. (once amended) [The] A pharmaceutical composition [of claim 57, wherein said compound is] comprising a pharmaceutically acceptable excipient or carrier and a compound selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4*H*-indolo[4,5-b]pyran;

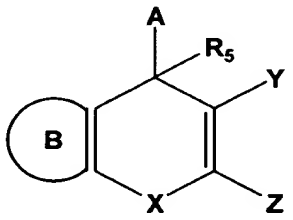
2-Amino-3-cyano-4-(3-cyanophenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran; and

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran.

65. (once amended) The pharmaceutical composition of claim 64, wherein said known cancer chemotherapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, [Herceptin] Herceptin®, [Rituxan] Rituxan® and alanosine.

75. (once amended) An indolopyran of Formula I:



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

B is optionally substituted indolo;

X is O;

Y is CN[, COR_7, CO_2R_7 or $CONR_xR_y$, wherein R_7, R_x and R_y are independently hydrogen, C_{1-10} alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R_x and R_y are taken together with the nitrogen to which they are attached to form a heterocycle];

Z is NR_8R_9, [$NHCOR_8$, $N(COR_8)_2$, $N(COR_8)(COR_9)$, $N{=}CHOR_8$ or $N{=}CHR_8$,] wherein R_8 and R_9 are independently H[,] or C_{1-4}alkyl [or aryl, or R_8 and R_9 are combined together with the group attached to them to form a heterocycle];

R_5 is hydrogen or C_{1-10} alkyl; and

A is optionally substituted [and is] C_{6-14}aryl[, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl].

78. (once amended) [The] A compound [of claim 77, wherein said compound is] selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran; and

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran.

New claims 79-81 have been added.